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COCAINE.

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COCAINE\* or Cucaine, the local anæsthetic, which has during the last few months obtained so great a notoriety, is obtained from the leaves of a South American plant called *Erythroxylon Coca*. The properties of the leaves of this plant have given rise to descriptions as celestial as those of De Quincey on opium. Mantegazza says "God is unjust for having made man live without coca; I would prefer a life of ten years with coca to one of ten thousand centuries without."

The first account of its uses is from the writings of Tschudi† in 1838; he says that the natives of Chili and Peru commence the use of it when quite young, and continue it till old age, preferring hunger to loss of coca. An Indian servant, sixty-two years old, worked day and night for five days, with the exception of two hours sleep daily, at a difficult task, with no food except that procured by the chewing of coca. This statement is corroborated by the experience of all the earlier writers on this subject.

Dr. Unanne mentions that during the siege of Pez all the inhabitants died of hunger, except the few who possessed coca leaves, and they scarcely suffered.

The natives always mix with the leaves a small quantity

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\* See *Practitioner*, xxxxiv. p. 56.

† Tschudi, *Reiseskizzen aus Peru, in den Jahren 1838-1842*, t. vi. St. Gallen, 1846.

of clipta, calling the mixture acullico. Clipta is the ash obtained by burning the dried twigs of various plants, and is supposed to act by liberating the active principle of the leaves, probably from the loose combination of cocaine with organic acids.

Moreno and Maiz\* in their research on coca say that the long use of it produces impairment of digestion, emaciation, jaundiced look, uncertain gait, fixity of the eyes, pale lips, tremblings, foul breath, and that the patient becomes more and more apathetic, loses sleep and appetite, and finally succumbs to dropsy and general marasmus.

Notwithstanding the extraordinary properties ascribed by travellers to this plant, it was not till 1859 that the active principle cocaine was separated by Niemann.† Lossen‡ says the best manner to obtain cocaine is to digest the smallest leaves with distilled water at  $60^{\circ}$ — $80^{\circ}$  C. ; the filtered solution is now precipitated with acetate of lead, the excess of lead is removed by sulphate of soda, the filtrate made weakly alkaline with soda, and shaken up with ether. To clear it, water is added, and sufficient quantity of hydrochloric acid, the solution is filtered, then precipitated with carbonate of soda, and crystallised out with hot alcohol. He obtained from the best leaves one-fifth per cent. by this means.

Chemically it has been assigned the formulas,  $C_{32}H_{20}NO_8$  and  $C_{17}H_{21}NO_4$ . It exists in very minute monoclinic prisms of a bitter taste. Lossen first showed that it required 704 parts of water to dissolve it. It is soluble in alcohol, chloroform, and ether.

The salts yet obtained are the hydrochlorate, acetate, citrate, and salicylate, of which the first has been the most extensively used. The dose of cocaine and its salts is  $\frac{1}{32}$  —  $1\frac{1}{2}$  grs.

The other substances obtained from the coca leaves consist of a volatile substance called hygrin, coca-tannin, ecgonine and a wax.

Physiologically, the best experiments published are the ones which were really the first systematically carried out,

\* Moreno and Maiz, *Recherches sur l'Erythroxylum Coca*. Paris. 1868.

† Niemann *Über eine neue organische Base in den Coca Blättern*. *Vierteljahrssch. für praktische Pharmacie*, Bd. ix.

‡ *Ann. Chem. Pharm.* 133, § 351.

namely, those by Hughes Bennett,\* in 1873, and for that reason I have mentioned his results fully. Their correctness has been substantiated by the exhaustive ones of Von Anrep† in 1880, though curiously he does not mention Bennett's thesis.

Schroff in 1862 mentioned in a lecture the property of cocaine in anæsthetising the mucous membrane of the tongue.

The chief conclusions drawn by Bennett‡ from his researches on cocaine and its allied alkaloids are the following:—

“In small, not fatal, doses, they produce cerebral excitement, and partial anæsthesia; in large fatal doses complete anæsthesia, tetanic spasms, and death. They paralyse the entire posterior columns of the spinal cord, and the peripheral sensory nerves, but do not affect the motor tract. They first increase, then impede, and lastly stop the respirations. They at first increase, and finally diminish both the force and frequency of the heart's contractions. They produce at first contraction, and afterwards dilatation of the capillaries and small bloodvessels, with stasis of the blood, indicating first irritation and subsequently paralysis of the vaso-motor nerves.” The other effects he mentions are myosis of the pupil, increased salivation, and tenesmus with a copious mucous discharge from the bowels; at the same time the temperature is at first slightly lowered and then increased.

Von Anrep's paper in 1880, referred to before, is the next one worth mentioning, recording as it does a large number of experiments on both cold- and warm-blooded animals. He mentions mydriasis as a constant symptom in warm-blooded animals, after both local and general application of the drug. He also notices the local anæsthesia of the skin after a hypodermic injection, and the loss of sensibility and taste after painting a portion of his tongue with a solution of the drug. He found the daily quantity and specific gravity of the urine varied within normal limits, that sometimes albumen and sugar appeared, but only in animals

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\* “An Experimental Inquiry into the Physiological Actions of Theine, Caffeine, Cocaine,” &c. (*Edin. Med. Journ.* vol. xix. p. 323).

† “Ueber die physiologische Wirkung des Cocaine,” von Dr. B. von Anrep (*Archiv für Phys. von Pflüger*, B. xxi. 1880, p. 38).

‡ *Op. cit.* pp. 325, 326.

which had suffered from long continued cramps and oppressed respiration.

Passing now from the literature of cocaine, we may enquire into the working of the drug medically and surgically. Our knowledge on the first heading is scanty. It has been given as a stomachic tonic, and from its action is surely likely to be a nervine tonic; the description of the excessive use of it graphically narrated above by Moreno and Maiz, would suggest its use in locomotor ataxia. But it is surgically that it has come so prominently before us lately, owing to the zeal of Dr. Karl Koller,\* who has drawn attention to its local anæsthetic action. It has been applied locally to most of the mucous membranes of the body. Its chief effects in ophthalmic practice may be studied by a consideration of the following cases and results obtained by myself from clinical experience.

As to the operations that I have performed under this anæsthetic, their small number makes me diffident in entering at great length into them. The salt of cocaine used in my experiments and operations has been in all cases the hydrochlorate in 2, 4, and 20 per cent. solutions.

The operations are twenty-two in number, viz., two extractions for senile cataract, three needlings for soft cataract, three iridectomies (one for glaucoma), two tenotomies for squint, three Meibomian cysts, slitting up three canaliculi, opening periosteal abscess of orbit, five removals of foreign bodies from the cornea; to these may be added passage of probes down the nasal duct six times.

Starting with the extraction cases, the first was a feeble old woman with chronic emphysema. Two instillations of 4 per cent. solution of cocaine were administered at five minutes interval, the anæsthesia of the cornea was perfect, but on seizing the iris she winced and complained of great pain; no pain felt after snipping off the iris, the operation being quite successful. The second case was a man of sixty-nine, and the strength of cocaine used was 20 per cent. I gave him six instillations at five minutes interval, and tried by drying the conjunctiva and cornea, to apply the drops at the upper part of the cornea selected for operation. The result was most perfect; he experienced no pain, though I made a free iridectomy in order to let out a quantity of soft matter.

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\* "On the Use of Cocaine for Producing Anæsthesia on the Eye," by Dr. Karl Koller (*Lancet*, December 6, 1884, p. 990).



The needle operations were painless, though all in small children. The iridectomies all experienced a certain amount of pain, especially the glaucoma case; this was probably due to the small amount of absorption into the anterior chamber due to the heightened tension, + 3, as the atrophied condition of the iris in such cases would surely tend to decrease the sensation.

The first squint was done after dropping the four per cent. solution on the lower lid twice. No pain was felt on cutting the conjunctiva or the capsule, but a good deal of pain on lifting the rectus.

In the second case, after two applications of the 4 per cent. solution to the conjunctiva, a few drops were injected by a syringe presumably into the internal rectus, and all the steps of the operation were painless. As to the Meibomian cysts, the first two were done by conjunctival instillation twice repeated, and pain was felt on clearing out the contents; in the third case an injection under the cyst was added and the patient complained of no pain. The periosteal abscess was treated by rubbing in three times a 4 per cent. chloroform solution, but with marked pain. In the operations on the the canaliculi, the first two were on the same patient, and for excessively small puncta and a great deal of secretion in the sac. Two instillations of 4 per cent. solution were used to the conjunctiva, and with the fine point of a hypodermic syringe a drop was passed into the punctum; this was slit up and another injection passed along the canaliculus, though pain was not very great, yet the patient winced a good deal.

The second case was in a nervous boy of ten, and the notes are interesting as showing well the anæsthetic effect of the alkaloid. I dropped carefully on the inner canthus a drop of 20 per cent. solution, and then carefully inserted into the puncture a cannula fitted on to a small syringe Messrs. Arnold, of Smithfield, have carefully made for me; a few drops were thus injected into the canaliculus, and after a minute the cannula pushed on and again injected. I then withdrew the cannula and slit the canaliculus freely up, keeping well towards the conjunctival surface. A piece of mucous membrane was then snipped off, and a probe, No. 6, passed into the duct without any pain. Thinking perhaps the boy had little æsthesia, and as it is an operation rarely needing a general anæsthetic, I proceeded to slit the other canaliculus up without injecting cocaine, but he

experienced so much pain that I finished the operation as in the first one under cocaine, waiting till the parts were dry.

In the foreign body cases, no pain was experienced, and in those for passage of lachrymal probes, the last two I have done after injection of the duct have been nearly painless, the slight pain experienced being probably due to tension from the size of the probe.

Looking at the results of these operations, and of others I have assisted at or watched, I should be inclined thoroughly to dry the part to be operated on, use, if possible, 20 per cent. solution, apply it as nearly as possible over the part, and if for the deeper structures, such as the iris, apply it five or six times at five minutes' interval. In iridectomy for glaucoma I think it will be useless unless one can inject the anterior chamber, and for this purpose Messrs. Arnold have constructed, at my suggestion, a small steel bent cutting needle; the stem being bored, this can be fitted on a syringe handle, and thus the solution can be injected into the anterior chamber. If deeper structures than the skin or mucous membrane are to be cut, I should advise exciting superficial local anæsthesia first, and then hypodermic or subfascial injection of the part.

I have practised it on myself and have produced local anæsthesia of the subcutaneous and deeper structures. The places I have tried have been the eyelid and twice in the thigh; in the former the complete anæsthesia spread more than usual owing probably to the loose subcutaneous tissue; in the latter the anæsthesia was very limited when I injected two minims of 2 per cent. solution, but was considerably greater on injecting ten minims. In the last case I intentionally pierced the muscle, which, on sensation returning, was seized with limited cramping pains. These lasted till the next day, so I shall not care to repeat this experiment.

A word of caution may be addressed in cases of foreign body, namely, that it increases the difficulty in extraction owing to the flaccidity of the cornea, and a great abrasion of cornea may be produced if care be not taken.

In the above-mentioned operation cases the earliest in each series were always done with 4 per cent., as only during the last three weeks have I been using 20 per cent. In none of the cases was any after trouble experienced at the site of the wound, owing to the anæsthesia produced;

and my last case of cataract, in which I used more than ever I had done before, has made a most perfect recovery, the wound healing in seven days, notwithstanding the patient's great age.

In several cases I have tested its efficacy in corneal ulcers with extreme photophobia, and have found it of great use in getting a child spontaneously to open its eyes, instead of as before going through the stage of struggling with it, and in the end scarcely being rewarded by a sight of the cornea, frightening the child, and alarming the mother.

As to its value in refraction the following case will best tell :—

Dr. R. J., æt 30, consulted me about his eyes, as his sight was getting gradually worse ; he had worn spectacles + 2D for some years for hypermetropia.

His pupils were so small that I could not satisfactorily estimate his refraction either by the direct method or retinoscopy, and added to this he was amblyopic in the right eye, so that I could not use homatropin. Acquiescing readily in my suggestion of cocaine, I put one drop of the 20 per cent. solution in his left eye. In ten minutes the pupil increased from two mm. to five mm. and his near and far points met ; eighteen minutes after this his pupil was 8·5 mm., and his accommodation was completely paralysed. With the greatest ease I estimated his hypermetropic astigmatism, and in another case should directly order glasses, but I was not then quite certain as to the working of the drug.

He told me the next day that the paralysis of accommodation disappeared one hour after it attained its maximum, and the pupil was fully contracted twelve hours after.

Mr. Butlin informs me that he has been using a 20 per cent. solution of cocaine for some weeks in his extensive throat department at St. Bartholomew's Hospital, and has been much pleased with its local action. He mentions especially one case of papilloma of the larynx, in which he had the greatest difficulty even in seeing the tumour before. After twice painting the mucous membrane of the larynx with the solution at four minutes' interval, he was enabled to see the application of the forceps to the tumour on the vocal cord, and easily to remove it. His own experiences on the inferior turbinated bone are recorded in the *Lancet* of November 29, 1884.



An interesting case of cocaine poisoning is mentioned by Ploss\* :—

An apothecary intending to commit suicide extracted twenty-four grammes of a crystallised substance from two pounds of coca leaves and administered it to himself in a glass of beer, afterwards taking two small glasses of brandy. For a time he felt quite well, and soon went to sleep but woke up with gripings of the stomach, burning pains in the palate, dryness of the mouth and throat, dizziness, great weakness of the whole body, perfect consciousness, pulse and temperature normal. After taking  $1\frac{1}{4}$  gr. of morphia he fell asleep and woke up quite well, though he did not pass urine for twenty-four hours.

The physiological effects I have noticed in my experiments were in most instances tried first on myself and some medical friends, and I think the best way to bring them forward will be to start with my first results, then give illustrations of each phase, and finally discuss the meaning of the effects.

My first experiment on myself was rough, being merely to induce anæsthesia, the other effects on the eye not being correctly noted.

Of the second I have the following notes :—

V.	}	R. $\frac{6}{6}$ : J. 1 at 22 cm.	Ref. emmetropic.
		L. $\frac{6}{6}$ : J. 1 at 22 cm.	Pupils 4 mm. and equal.
11.38 A.M.		Cocaine 4 per cent. solution into left eye.	
11.43		Cocaine.	
11.41		Cocaine.	Pupil 4.5 mm. V. same.
12	M.	Cocaine.	Pupil 5 mm. V. same.
12.10 P.M.		Cocaine.	Pupil 7.5 mm.
12.15		Cocaine.	Pupil 7.5 mm. J. 4 at 22 cm.
12.25			Pupil 7.5 mm. J. 12 at 22 cm.
			+4 D; J. 1 at 22 cm.

The loss of accommodation lasted three-quarters of an hour.

The points noted were :—

1. Dilatation of pupils though acting to light, and to the movements of accommodation.

2. Complete anæsthesia of cornea and conjunctiva in fifteen minutes, the anæsthesia limited to the conjunctival margin of the lids, any traction on the lashes giving rise to pain.

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\* Varge's *Zeitschr.* v. f. 11 5, p. 222, 1863.